REMARKS

Claims 1-48 are pending in this application. Claim 30 has been canceled and claims 1-28 and 35-48 have been withdrawn, leaving claims 29 and 31-34 remaining. Claim 30 has been canceled in the expectation that the amendments will place this application in condition for allowance. The subject matter of canceled claim 30 has been incorporated into the independent claim 29, from which it depends.

The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the claim amendments is found in claims 1-48 as originally filed, and elsewhere throughout the specification and claims. Accordingly, entry of the amendments is respectfully requested.

1. Election/Restriction

The Office Action requires restriction to one of the following inventions under 35 U. S. C. §121:

> I. Claims 1, 3, 5, 7, 9, 11, 35 and 37, drawn to a nucleotide sequence encoding a lectin isolated from Korean mistletoe, an isoform of A chain of the lectin, or an isoform of B chain of the lectin, classified in class 536, subclass 23.1.
>
> II. Claims 2, 4, 6, 8, 10, 12-18, 36, 38, 45 and 46, drawn to a lectin isolated from Korean mistletoe, or a lectin peptide involved in biosynthesizing lectin; and a pharmaceutical composition comprising the lectin, classified in class 530, subclass 396, and class 514, subclass 2.
>
> III. Claims 19-22, drawn to a method of preparing a lectin isolated from Korean mistletoe using

immuno-affinity column chromatography, classified in class 530, subclasses 396 and 387.1.

IV. Claims 23-28, drawn to a method of enhancing immunity, comprising administering to an animal a lectin isolated from Korean mistletoe, classified in class 530, subclass 396.

V. Claims 29-34, drawn to a method of effectuating antitumor activity, comprising administering to an animal a lectin isolated from Korean mistletoe, classified in class class 530, subclass 396.

VI. Claim 39, drawn to a method of inducing IFN-y, comprising administering to an animal Korean Mistletoe Heparin Binding Protein (KMHBP), classified in class 530, and subclass 350.

VII. Claims 40 and 47, drawn to a pharmaceutical composition comprising a protein fraction of KMHBP, and a method of preparing the protein fraction of KMHBP, classified in class 530, subclass 350.

VIII. Claim 41, drawn to a method of enhancing immunity, comprising administering to an animal a protein fraction of KMHBP, classified in class 530, subclass 350.

IX. Claims 42, 44 and 48, drawn to a mixture of KML-C and KMHBP, a pharmaceutical composition comprising the mixture of KML-C and KMHBP, and a method of preparing the mixture, classified in class 530, subclasses 350 and 396.

X. Claim 43, drawn to a method of enhancing immunity and effectuating antitumor activity, comprising administering a mixture of KML-C and KMHBP, classified in class 530, subclasses 350 and 396.

Applicants affirm the provisional election to prosecute the invention of Group V, claims 29-34, with traverse, made during a telephone conversation between Examiner Hope Robinson and Sheldon McGee on May 10, 2002.

Applicants respectfully traverse the restriction requirement.

First, the restriction requirement is traversed because it omits "an appropriate explanation" as to the existence of a "serious burden" if a restriction were not required. See MPEP 803.

Regardless of any differences which may exist between the inventions set forth in the claims of Groups II-V, IX, and X, a complete and thorough search for the invention set forth in any one of the Groups would require searching the art areas appropriate to the other Groups. As the Examiner concedes, all of Groups II-V, IX, and X fall under class 530, subclass 396. Similarly, all of Groups VI-X fall under class 530, subclass 350. Several of the Inventive Groups identified by the Examiner are related by bridging claims generic to the claims within each Group, for example, Group IV, relating to claims 23-28, drawn to a method of enhancing immunity, is sub-generic to the elected Group V, relating to claims 29-34. Since a search of each of the inventions of these sets of Inventive Groups would be coextensive, it would not be a serious burden upon the Examiner to examine all, or at least substantially more, of the claims in this application.

Furthermore, applicants have paid a filing fee for an examination of all the claims in this application. If the Examiner refuses to examine the claims paid for when filing this application and persists in requiring applicants to file divisional applications for each of the groups of claims, the Examiner would essentially be forcing applicants to pay duplicative fees for the non-elected or withdrawn claims, inasmuch as the original filing fees for the claims (which would be later prosecuted in divisional applications) are not refundable.

2. Objections to the Specification

The Office Action objects to the Specification because of the following informalities:

> The specification indicates Fig. 33 and Fig. 34 show the nucleotide sequence and the amino acid sequence of KML-I1U and KML-IIL, respectively (pages 7, 8 and 49), however, Figs. 33 and 34 have not been provided. Appropriate correction is required.
>
> Tables 9a, 9b, 9c, and 9d show amino acid sequence comparison of Korean Mistletoe lectins, European Mistletoe lectins and other related lectins. However, the numbering of amino acid residues is not provided in the sequence comparison (especially in the A chain), it is not clear where is the sequence homology among various sequences. The specification does not define GI in Table 9a. Appropriate correction is required.

Applicants have amended the Specification to correct obvious errors in the description of Figures 33-36, specifically to remove reference to sequence listings in the Brief Descriptions of Figures 33 and 34, and to renumber the Brief Descriptions of Figures 35 and 36 to correctly read Figures 33 and 34, corresponding to the actual drawings. As the sequences are now included in a separate section of the application, they are no longer in the description of the drawings.

Regarding the numbering of amino acid residues in Tables 9a, 9b, 9c, and 9d, Applicants respectfully traverse the objection because: (1) the numbering of amino acid residues in the amino acid sequence comparison is irrelevant to the patentability of the inventive subject matter; (2) the Specification explains the

content of Tables 9a-d to the extent required; and (3) the corrections suggested by the Examiner would in part constitute new matter and cannot be made. "GI" in Table 9a is corrected to "CI."

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the objections to the Specification.

2. Rejection of Claims 29-34 under 35 U.S.C. §112, second paragraph

The Office Action rejects claims 29-34 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons:

> Claims 29-34 are indefinite because the claims lack essential steps in the method of effectuating antitumor activity in animals. The omitted steps are the effective amount of lectin from Korean misletoe administered and the outcome for the treatment. Claims 30-34 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Applicants thank the Examiner for her helpful comments. Applicants have amended claim 29 to state "an effective amount" and to state the alternative treatments outcomes described in the Specification.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 29-34.

3. Rejection of Claims 29-31 and 33 under 35 U.S.C. §102

The Office Action rejects claims 29, 30, 31, and 33 under 35 U.S.C. §102(b), as being anticipated by Applicants earlier publication, Yoon, et al. (International J. Immunopharmacology 20, 163-172 (April-May 1998)), for the reasons that:

> Yoon et al. teach an aqueous extract (KM-110) prepared from *Viscum album coloratum* (Korean mistletoe) inhibits tumor metasis in experimental lung metastatsis of B16-BL6 melanoma or colon 26-M3.1 carcinoma cells (Table 1), and spleen metastasis of L5178Y-ML25 lymphoma cells (Table 2) when administered of KM-110 (100 μg) before tumor inoculation (pages 166-167; claims 29, 30, 31 and 33). Claims 29, 30, 31 and 33 are anticipated by the reference because the extract of KM-110 containing isolated lectins as shown in the specification has antitumor activity, and claims 30, 31 and 33 recite the lectin of KML-IIU and/or KML-IIL, but, no characteristic or property of the protein is indicated, thus any lectin having antitumor activity and isolated from Korean mistletoe is considered as KML-IIU or KML-IIL.

Applicants respectfully traverse this rejection on the basis that Yoon, et al. fails to teach the claimed subject matter. As the Examiner admits, Yoon, et al. teaches the use of KM-110. As amended, pending claims 29-34 relate to KML-IIU and KML-IIL. Contrary to the Office Action, and as discussed throughout the Specification, KML-IIU and KML-IIL are <u>not</u> the same as KM-110. Thus, the Examiner's conclusion that "any lectin having antitumor activity and isolated from Korean mistletoe is considered as KML-IIU or KML-IIL," is unsupported by the disclosure in the cited reference and contradicted by Applicants disclosure.

To constitute anticipation under 35 U.S.C. §102, all material elements of a claim must be formed in one prior art source. In re Marshall, 577 F.2d 301, 198 USPQ 344 (CCPA 1978); In re Kalm, 378 F.2d 959, 154 USPQ 10 (CCPA 1967). Yoon's disclosure of KM-110 is not tantamount to a disclosure of isolated KML-IIU and/or KML-IIL. Thus, in the absence of any teaching in Yoon, et al. that KM-110 would necessarily teach KML-IIU and/or KML-IIL, Yoon, et al. does not anticipate the present claims.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 29, 30, 31, and 33.

4. Rejection of Claims 29-31 and 33 under 35 U.S.C. §103

The Office Action rejects claims 29, 30, 31, and 33 under 35 U.S.C. §103, as being unpatentable over Khwaja et al. (Proc. Am. Assoc. Cancer Res. Annu. Meet. 28, 303 (1987)) taken with Khwaja (U. S. Patent 5,565,200), for the reasons that:

> Khwaja et al. teach a lectin, which is isolated from the aqueous extract of Viscum album, Sepharose 4B column, and eluting with 0.15 M lactose in 0.5 M NaCl, has antiocancer activity against the growth of leukemia L1210 cells in culture with IC50 of 0.66 ng/ml, and the SDS gel electrophoresis of lectin shows two major bands 29 and 36 kDa (whole abstract; claims 29, 30, 31 and 33). However, Khwaja et al. do not dislose the administration of the lectin from Korean mistletoe to an animal. Khwaja teaches aqueous extracts from Korean mistletoe, which contain lectins, viscotoxins and alkaloidal compounds, exhibit antileukemia activity against L1210 cells and anticancer activity in animals bearing tumor cells (column 11, line 57-column 12, line 35; Example 1; claim 12 of the 200'

> patent). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to use the isolated lectin taught by Khwaja et al. in treating an animal having cancer because the use of an active ingredient in the extract would provide an alternative method for effective treatment of cancer. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made. Claims 30, 31 and 33 recite the lectin of KML-IIU and/or KML-IIL, but, no characteristic or property of the protein is indicated, thus any lectin having antitumor activity and isolated from Korean mistletoe is considered as KML-IIU or KML-IIL.

Applicants respectfully traverse this rejection. As the Examiner admits, Khwaja, et al. teaches the use of two lectins characterized as having major bands at 29 kDa and 36 kDa. Khwaja, et al. is deficient in teaching the inventive subject matter because it does not dislose the administration of the lectin from Korean mistletoe to an animal. The Khwaja patent teaches aqueous extracts from Korean mistletoe exhibit antileukemia activity against L1210 cells and anticancer activity in animals bearing tumor cells.

As shown throughout the Specification, KML-IIU and KML-IIL are lectins having specific sequences and properties which are clearly distinguishable from either Khwaja, et al. or the Khwaja patent. Thus, contrary to the Examiner's conclusion that "any lectin having antitumor activity and isolated from Korean mistletoe is considered as KML-IIU or KML-IIL," is unsupported by the disclosure in the cited references and contradicted by Applicants disclosure.

To establish a *prima facie* case, the PTO must satisfy three requirements. First, the prior art reference must teach or suggest all the limitations of the claims. *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). Second, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Lastly, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991).

The cited references meet none of these requirements. Particularly notable is the failure to teach or suggest all the limitations of the claims: neither Khwaja, et al. nor the Khwaja patent teach or suggest isolated KML-IIU and KML-IIL. Lacking this element of Applicants' claims, there is no motivation to modify the teaching of either cited reference to produce the invnetive subject matter. Nor is there a reasonable expectation of success without the required teaching of either KML-IIU or KML-IIL, or some motivation to modify Khwaja, et al. or the Khwaja patent to use KML-IIU or KML-IIL. Thus, in the absence of any teaching or

suggestion in Khwaja, et al. or the Khwaja patent that KML-IIU or KML-IIL would be useful for treating tumors, the claims of the present application cannot be obvious over Khwaja, et al. or the Khwaja patent, either alone or in combination.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 29, 30, 31, and 33.

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of remaining claims 29-34, to withdraw, at least in part, the restricion requirement, and to allow all pending claims presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,

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